SMARCB1 gene

SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1

Normal Function

The *SMARCB1* gene provides instructions for making a protein that forms one piece (subunit) of several different SWI/SNF protein complexes. SWI/SNF complexes regulate gene activity (expression) by a process known as chromatin remodeling. Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Through their ability to regulate gene activity, SWI/SNF complexes are involved in many processes, including repairing damaged DNA; copying (replicating) DNA; and controlling the growth, division, and maturation (differentiation) of cells. The SMARCB1 protein and other SWI/SNF subunits are thought to act as tumor suppressors, which keep cells from growing and dividing too rapidly or in an uncontrolled way.

The role of the SMARCB1 protein within the SWI/SNF complex is not fully understood.

Health Conditions Related to Genetic Changes

Coffin-Siris syndrome

At least five mutations in the *SMARCB1* gene have been found to cause Coffin-Siris syndrome. This condition is characterized by delayed development, abnormalities of the fifth (pinky) fingers or toes, and characteristic facial features that are described as coarse. These *SMARCB1* gene mutations change or remove single protein building blocks (amino acids) in the SMARCB1 protein. Although it is unclear how these changes affect SWI/SNF complexes, researchers suggest that *SMARCB1* gene mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts several cell activities, which could explain the diverse signs and symptoms of Coffin-Siris syndrome. People with Coffin-Siris syndrome do not appear to have an increased risk of cancer (see below).

schwannomatosis

More than two dozen mutations in the *SMARCB1* gene have been found in people with schwannomatosis, a disorder characterized by multiple noncancerous (benign) tumors called schwannomas that grow on nerves. This type of tumor arises from

Schwann cells, which are specialized cells that normally form an insulating layer around the nerve.

SMARCB1 gene mutations associated with schwannomatosis lead to production of an altered SMARCB1 protein whose function is reduced but not eliminated. The altered protein is less able to control how cells grow and divide, which can allow tumors to develop. However, it is unknown why these mutations are predominantly associated with schwannomas, instead of other tumor types, in people with schwannomatosis.

It appears that mutations in *SMARCB1* alone are not enough to trigger the development of schwannomas. Additional genetic changes (somatic mutations) that are acquired during a person's lifetime and are present only in certain cells may also be required for schwannomas to form.

Some people who have a mutation in the *SMARCB1* gene never develop tumors, which is a situation known as reduced penetrance.

other disorders

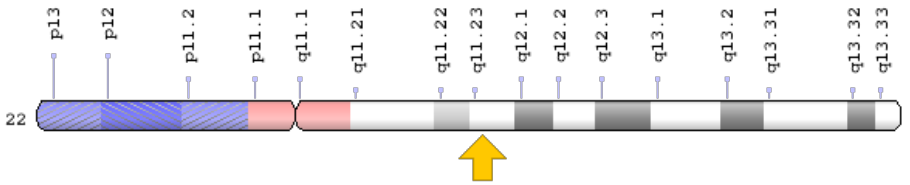
Mutations in the *SMARCB1* gene cause rhabdoid tumor predisposition syndrome (RTPS). Individuals with this condition have an increased risk of developing aggressive cancerous growths called rhabdoid tumors, which form in the brain (where they are often called atypical teratoid/rhabdoid tumors) and in the kidney (where they are often called malignant rhabdoid tumors). These tumors usually occur in infants and young children. Some children with RTPS also develop schwannomas. RTPS is caused by a mutation in the *SMARCB1* gene that is present in cells throughout the body (called a germline mutation). An additional somatic mutation that deletes the normal copy of the gene is needed for tumors to develop. In combination, the germline and somatic mutations lead to the absence of SMARCB1 protein.

Somatic mutations in both copies of the *SMARCB1* gene, which result in the absence of SMARCB1 protein, cause noninherited (sporadic) rhabdoid tumors in children. The mechanism by which germline or somatic *SMARCB1* gene mutations lead to rhabdoid tumors is unknown.

Chromosomal Location

Cytogenetic Location: 22q11.23, which is the long (q) arm of chromosome 22 at position 11.23

Molecular Location: base pairs 23,786,931 to 23,834,518 on chromosome 22 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BAF47
- BRG1-associated factor 47
- hSNF5
- hSNFS
- INI1
- integrase interactor 1 protein
- MRD15
- PPP1R144
- RDT
- RTPS1
- Sfh1p
- SNF5
- SNF5 homolog
- SNF5_HUMAN
- SNF5L1
- Snr1

- sucrose nonfermenting, yeast, homolog-like 1
- SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): ATP-Driven Chromatin Remodeling Machines Change Nucleosome Structure
  https://www.ncbi.nlm.nih.gov/books/NBK26834/#A644
- Molecular Biology of the Cell (fourth edition, 2002): Chromosomal DNA and Its Packaging in the Chromatin Fiber
  https://www.ncbi.nlm.nih.gov/books/NBK26834/

GeneReviews

- Coffin-Siris Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK131811

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SMARCB1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- RHABDOID TUMOR PREDISPOSITION SYNDROME 1
  http://omim.org/entry/609322
- SWI/SNF-RELATED, MATRIX-ASSOCIATED, ACTIN-DEPENDENT REGULATOR OF CHROMATIN, SUBFAMILY B, MEMBER 1
  http://omim.org/entry/601607

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/SMARCB1ID169.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SMARCB1%5Bgene%5D
- HGNC Gene Family: Protein phosphatase 1 regulatory subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/694

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11103
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6598
- UniProt
  http://www.uniprot.org/uniprot/Q12824

Sources for This Summary

- Biegel JA, Tan L, Zhang F, Wainwright L, Russo P, Rorke LB. Alterations of the hSNF5/INI1 gene in central nervous system atypical teratoid/rhabdoid tumors and renal and extrarenal rhabdoid tumors. Clin Cancer Res. 2002 Nov;8(11):3461-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12429635
- Bruggers CS, Bleyl SB, Pysher T, Barnette P, Afify Z, Walker M, Biegel JA. Clinicopathologic comparison of familial versus sporadic atypical teratoid/rhabdoid tumors (AT/RT) of the central nervous system. Pediatr Blood Cancer. 2011 Jul 1;56(7):1026-31. doi: 10.1002/pbc.22757.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20848638
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3210729/
- Eaton KW, Tooke LS, Wainwright LM, Judkins AR, Biegel JA. Spectrum of SMARCB1/INI1 mutations in familial and sporadic rhabdoid tumors. Pediatr Blood Cancer. 2011 Jan;56(1):7-15. doi: 10.1002/pbc.22831.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21108436
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086793/
- Hadfield KD, Newman WG, Bowers NL, Wallace A, Bolger C, Colley A, McCann E, Trump D, Prescott T, Evans DG. Molecular characterisation of SMARCB1 and NF2 in familial and sporadic schwannomatosis. J Med Genet. 2008 Jun;45(6):332-9. doi: 10.1136/jmg.2007.056499. Erratum in: J Med Genet. 2008 Sep;45(9):608.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18285426
- Hulsebos TJ, Plomp AS, Wolterman RA, Robanus-Maandag EC, Baas F, Wesseling P. Germline mutation of INI1/SMARCB1 in familial schwannomatosis. Am J Hum Genet. 2007 Apr;80(4):805-10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17357086
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1852715/
- OMIM: SWI/SNF-RELATED, MATRIX-ASSOCIATED, ACTIN-DEPENDENT REGULATOR OF CHROMATIN, SUBFAMILY B, MEMBER 1
  http://omim.org/entry/601607
- Santen GW, Kriek M, van Attikum H. SWI/SNF complex in disorder: SWItching from malignancies to intellectual disability. Epigenetics. 2012 Nov;7(11):1219-24. doi: 10.4161/epi.22299. Epub 2012 Sep 25. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23010866
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3499322/

- Tsurusaki Y, Okamoto N, Ohashi H, Kosho T, Imai Y, Hibi-Ko Y, Kaname T, Naritomi K, Kawame H, Wakui K, Fukushima Y, Homma T, Kato M, Hiraki Y, Yamagata T, Yano S, Mizuno S, Sakazume S, Ishii T, Nagai T, Shiina M, Ogata K, Ohta T, Niikawa N, Miyatake S, Okada I, Mizuguchi T, Doi H, Saitsu H, Miyake N, Matsumoto N. Mutations affecting components of the SWI/SNF complex cause Coffin-Siris syndrome. Nat Genet. 2012 Mar 18;44(4):376-8. doi: 10.1038/ng.2219.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22426308
- Wieczorek D, Bögershausen N, Beleggia F, Steiner-Haldenstätt S, Pohl E, Li Y, Milz E, Martin M, Thiele H, Altmüller J, Alanay Y, Kayserili H, Klein-Hitpass L, Böhringer S, Wollstein A, Albrecht B, Boduroglu K, Caliebe A, Chrzanowska K, Cogulu O, Cristofoli F, Czeschik JC, Devriendt K, Dotti MT, Elcioglu N, Gener B, Goecke TO, Krajewska-Walasek M, Guillén-Navarro E, Hayek J, Houge G, Kilic E, Simsek-Kiper PÖ, López-González V, Kuechler A, Lyonnet S, Mari F, Marozza A, Mathieu Dramard M, Mikat B, Morin G, Morice-Picard F, Ozkinay F, Rauch A, Renieri A, Tinschert S, Utine GE, Vilain C, Vivarelli R, Zweier C, Nürnberg P, Rahmann S, Vermeesch J, Lüdecke HJ, Zeschnigk M, Wollnik B. A comprehensive molecular study on Coffin-Siris and Nicolaides-Baraitser syndromes identifies a broad molecular and clinical spectrum converging on altered chromatin remodeling. Hum Mol Genet. 2013 Dec 20;22(25):5121-35. doi: 10.1093/hmg/ddt366.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23906836
- Wilson BG, Roberts CW. SWI/SNF nucleosome remodellers and cancer. Nat Rev Cancer. 2011 Jun 9;11(7):481-92. doi: 10.1038/nrc3068. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21654818

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